CLAIMS

What is claimed is:

1. An adenovirus vector comprising an adenovirus gene under the transcriptional control of a transcriptional regulatory element (TRE) comprising a minimal promoter and a hypoxia responsive element (HRE).

2. The adenovirus vector of claim 1, wherein the adenovirus gene is selected from the group consisting of an E1A gene, an E1B gene, an E2A gene, an E2B gene, and an E4 gene.

3. The adenovirus vector of claim 1, further comprising a second adenovirus gene under the transcriptional control of the TRE.

4. The adenovirus vector of claim 1, wherein the minimal promoter is selected from the group consisting of the cytomegalovirus (CMV) minimal promoter, the human β-actin minimal promoter, the human EF2 minimal promoter, and the adenovirus E1B minimal promoter.

5. The adenovirus vector of claim 4, wherein the CMV minimal promoter comprises SEQ ID NO: 1.

6. The adenovirus vector of claim 1, wherein the HRE is derived from the human vascular endothelial growth factor (VEGF) promoter.

7. The adenovirus vector of claim 6, wherein the HRE comprises SEQ ID NO: 2.

8. The adenovirus vector of claim 7, wherein the HRE comprises five tandem copies of SEQ ID NO: 2.

9. The adenovirus vector of claim 1, further comprising a transgene.

10. The adenovirus vector of claim 9, wherein the transgene is a second adenovirus gene.

11. The adenovirus vector of claim 9, wherein the transgene encodes an immunostimulatory molecule.

12. The adenovirus vector of claim 11, wherein the immunostimulatory molecule is selected from the group consisting of IL2 and IL12.

13. The adenovirus vector of claim 9, wherein the transgene is a suicide gene.

14. The adenovirus vector of claim 13, wherein the suicide gene is selected from the group consisting of a TNF-α gene, a Trail gene, a Bax gene, an HSV-tk gene, a cytosine deaminase gene, a p450 gene, and a diphtheria toxin gene, an s-Flt1 gene, and an ex-Flk1 gene.

15. A composition comprising the adenovirus vector of claim 1.

16. The composition of claim 15, further comprising a pharmaceutically acceptable carrier.

17. A method for suppressing tumor growth, the method comprising contacting a hypoxic cell in a tumor with the adenovirus vector of claim 1, whereby the vector enters the cell and inhibits tumor growth.

18. The method of claim 17, wherein the contacting results from administering the adenovirus vector via intratumoral injection.

19. The method of claim 17, wherein the contacting results from administering the adenovirus vector by intravenous injection.

20. The method of claim 17, further comprising exposing the tumor to a therapeutically effective amount of a second treatment, the second treatment chosen from the group consisting of ionizing radiation, chemotherapy, and photodynamic therapy.

21. A host cell comprising the adenovirus vector of claim 1.

22. A method for conferring selective cytotoxicity on a target cell, the method comprising contacting a cell that allows an HRE to function with the adenovirus of claim 1, whereby the adenovirus vector enters the cell.

23. A method for selectively propagating an adenovirus in target tissue expressing HIF-1, the method comprising contacting the target tissue with an adenovirus according to claim 1, whereby the adenovirus is propagated to a titer of at least 1.0×10^7 pfu/ml.

24. A method of inhibiting growth of a target tissue, the method comprising:

(a) contacting a hypoxic cell in a target tissue with a first adenovirus vector, whereby the first adenovirus vector enters the cell; and

(b) contacting the hypoxic cell with a replication deficient adenovirus vector, whereby the replication deficient adenovirus vector enters the cell.

25. The method of claim 24, wherein the target tissue is a tumor.

26. The method of claim 24, wherein the first adenovirus vector comprises an adenovirus gene under the transcriptional control of a TRE comprising an HRE.

27. The method of claim 24, wherein the replication deficient adenovirus vector comprises a second gene.

28. The method of claim 27, wherein the replication deficient adenovirus vector comprises a second gene under the transcriptional control of a constitutive promoter.

29. The method of claim 27, wherein the replication deficient adenovirus vector comprises a second gene under the transcriptional control of a TRE comprising an HRE.

30. The method of claim 24, wherein:

(a) the first adenovirus vector comprises at least two essential adenovirus genes under the transcriptional control of a TRE comprising an HRE; and,

(b) the replication deficient adenovirus vector is deficient in at least two of the essential adenovirus genes under the transcriptional control control of a TRE comprising an HRE in the first adenovirus vector.

31. The method of claim 30, wherein the two essential adenovirus genes are each selected from the group consisting of an E1A gene, an E1B gene, an E2A gene, an E2B gene, and an E4 gene.

32. The method of claim 27, wherein the second gene is a suicide gene.

33. The method of claim 32, wherein the suicide gene is chosen from the group consisting of a TNF-α gene, a Trail gene, a Bax gene, an HSV-tk gene, a cytosine deaminase gene, a p450 gene, and a diphtheria toxin gene, an s-Flt1 gene, and an ex-Flk1 gene.

34. The method of claim 27, wherein the second gene encodes an immunostimulatory molecule.

35. The method of claim 32, wherein the immunostimulatory molecule is selected from the group consisting of IL2 and IL12.

36. The method of claim 24, further comprising exposing the target tissue to a therapeutically effective amount of a second treatment, the second treatment chosen from the group consisting of ionizing radiation, chemotherapy, and photodynamic therapy.